EQUIVALENTS

[0257] The present technology is not to be limited in terms of the particular embodiments described in this application, which are intended as single illustrations of individual aspects of the present technology. Many modifications and variations of this present technology can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. Functionally equivalent methods and apparatuses within the scope of the present technology, in addition to those enumerated herein, will be apparent to those skilled in the art from the foregoing descriptions. Such modifications and variations are intended to fall within the scope of the appended claims. The present technology is to be limited only by the terms of the appended claims, along with the full scope of equivalents to which such claims are entitled. It is to be understood that this present technology is not limited to particular methods, reagents, compounds compositions or biological systems, which can, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

1. A method for treating or preventing $BRAF^{V600E}$-associated neurodegenerative disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a BRAF, MEK, and/or CSF-1R inhibitor, or a pharmaceutically acceptable salt thereof.

2. The method of claim **1**, wherein at least a portion of the resident macrophages in the central nervous system of the subject are $BRAF^{V600E+}$.

3. A method for treating or preventing $BRAF^{V600E}$-associated neurodegenerative disease comprising:

(a) isolating resident macrophages from a neuronal environment of the subject;

(b) determining whether the resident macrophages express $BRAF^{V600E+}$; and

(c) administering to the subject a therapeutically effective amount of a BRAF, MEK, and/or CSF-1R inhibitor, or a pharmaceutically acceptable salt thereof, when the isolated resident macrophages express $BRAF^{V600E+}$.

4. The method of claim **1**, wherein the neurodegenerative disease is characterized by one or more of impaired cognitive functions, dementia, ataxia, dysarthria, reduced motor coordination and synchrony as compared to a normal control subject, paralysis, microglia accumulation, astrogliosis, microglia phagocytosis, demyelination, neuronal loss in the central nervous system, synaptic loss in the central nervous system, and amyloid precursor protein (APP) deposits in the brain.

5. The method of claim **1**, wherein the BRAF inhibitor is selected from the group consisting of vemurafenib, dabrafenib, encorafenib, PLX7904, PLX8394, GDC-0879, LGX818, and PLX4720, the MEK inhibitor is selected from the group consisting of AZD8330, refametinib, E6201, MEK162 (binimetinib), PD0325901, pimasertib, R04987655, selumetinib, TAK-733, GDC-0623, WX-544, cobimetinib, and trametinib, and the CSF-1R inhibitor is selected from the group consisting of GW2580, BLZ945, pexidartinib (PLX3397), ARRY-382, PLX7486, and JNJ-40346527.

6. The method of claim **1**, wherein the route of administration of the BRAF, MEK, or CSF-1R inhibitor is parenteral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intranasal, intracerebral, intrathecal, intravaginal, transdermal, rectal, by inhalation, or topical.

7. The method of claim **1**, wherein treatment of the neurodegenerative disease comprises one or more of improving cognitive functions, reducing dementia, reducing ataxia, reducing dysarthria, increasing motor coordination and synchrony, relieving paralysis, reducing microglia accumulation, reducing astrogliosis, reducing microglia phagocytosis, reducing demyelination, reducing neuronal loss, reducing synaptic loss, or reducing amyloid precursor protein (APP) expression in the brain as compared to an untreated control.

8. The method of claim **5**, wherein the BRAF inhibitor is vemurafenib.

9. The method of claim **5**, wherein the BRAF inhibitor is PLX4720.

10. A method for treating or preventing neurodegenerative disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a PI 3-kinase inhibitor, or a pharmaceutically acceptable salt thereof, wherein at least a portion of the resident macrophages in the central nervous system of the subject comprise one or more PI 3-kinase mutations.

11. The method of claim **10**, wherein at least a portion of the resident macrophages in the central nervous system of the subject are $PIK3CA^{H1047R+}$.

12. The method of claim **10** or **11**, wherein the neurodegenerative disease is characterized by one or more of impaired cognitive functions, dementia, ataxia, dysarthria, reduced motor coordination and synchrony as compared to a normal control subject, paralysis, microglia accumulation, astrogliosis, microglia phagocytosis, demyelination, neuronal loss in the central nervous system, synaptic loss in the central nervous system, and amyloid precursor protein (APP) deposits in the brain.

13. The method of claim **10**, wherein the PI 3-kinase inhibitor is selected from the group consisting of idelalisib, BKM120, GDC-0980, PF-04691502, XL147, IPI-145, BYL719, SF1126, BAY80-6946, GSK2126458, NVP-BEZ235, GDC-0941, PX-866, XL765, and ZSTK474.

14. The method of claim **10**, wherein the route of administration of the PI 3-kinase inhibitor is parenteral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intranasal, intracerebral, intrathecal, intravaginal, transdermal, rectal, by inhalation, or topical.

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